

535. *Halogeno-1,4-dioxans and Their Derivatives. Part III.*<sup>1</sup> *Inter-action of trans-2,3-Dichloro-1,4-dioxan and Amines.*

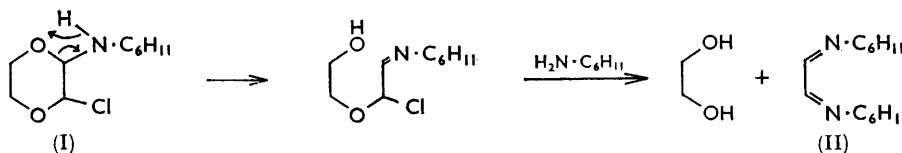
By L. A. CORT and N. R. FRANCIS.

Under anhydrous conditions *trans*-2,3-dichloro-1,4-dioxan acts effectively as a source of glyoxal in reaction with cyclohexylamine and with ethylenediamine; reaction with methylaniline is merely one of dehydrohalogenation. 2-Chloro-5,6-dihydro-1,4-dioxin reacts with acetamide to give acetonitrile and 1,4-dioxan-2-one.

In continuation of experiments<sup>1,2</sup> in which it was hoped that substitution of *trans*-2,3-dichloro-1,4-dioxan would lead to products by establishment of C-N linkages, the chloro-ether has been treated with methylaniline, with ethylenediamine, with cyclohexylamine, and with potassium phthalimide.

With methylaniline at elevated temperatures, exothermic reactions ensued with production of large proportions of black intractable materials, presumably largely polymers of 2-chloro-5,6-dihydro-1,4-dioxin. In ethanol at room temperature reaction occurred slowly, but the only product isolated (and purified with difficulty) was methylaniline hydrochloride. No product was found corresponding to the 2,3-bismethylphenylamino-1,4-dioxan suggested<sup>2</sup> to be formed in this way. The dichlorodioxan did not react with potassium phthalimide in dimethylformamide at 90°.

With cyclohexylamine in ethanol at room temperature, the chloro-ether slowly reacted to give *sym*-biscyclohexyliminoethane (II). Since it has been established<sup>1</sup> that the dichlorodioxan does not rearrange appreciably to glyoxal, even when heated, it is



probable that substitution does occur, and that the intermediate (I) breaks down as shown. Ethylene glycol was also detected in the product under conditions where it could not have arisen by hydrolysis of the dichlorodioxan. 1,2-Dichloro-1,2-diethoxyethane similarly<sup>3</sup> condensed with *o*-phenylenediamine, but this reaction occurred in ether; in alcohol the reaction took another course.

With ethylenediamine in ethanol, 1,2-dichloro-1,2-diethoxyethane gives a product to which the structure decahydropyrazino[2,3-*b*]pyrazine has been assigned.<sup>4,5</sup> (There is evidence<sup>6</sup> that 2-methylimidazolidines tautomerise to open-chain isomers.) The dichlorodioxan also gives this product, the melting point of which is somewhat variable (see Experimental section).

Although no substituted 2,3-diamino-1,4-dioxans have been obtained as yet from 2,3-dichloro-1,4-dioxan, the dibenzoyl derivative of the amine has been prepared<sup>7</sup> in a very indirect manner.

It was reported<sup>1</sup> that *trans*-2,3-dichloro-1,4-dioxan and acetamide react exothermically when heated, giving 2-chloroethyl acetate. Since the dichlorodioxan is known<sup>8</sup> to yield 2-chloro-5,6-dihydro-1,4-dioxin by thermal elimination of hydrogen chloride, the reaction

<sup>1</sup> Part II, Cort and Francis, *J.*, 1963, 3510.

<sup>2</sup> Elderfield, "Heterocyclic Compounds," Chapman and Hall, London, 1957, Vol. VI, p. 17.

<sup>3</sup> Baganz and Pflug, *Chem. Ber.*, 1956, **89**, 689.

<sup>4</sup> Baganz, Domaschke, and Kirchner, *Chem. Ber.*, 1961, **94**, 2676.

<sup>5</sup> Chitwood and McNamee, U.S.P. 2,345,237/1944.

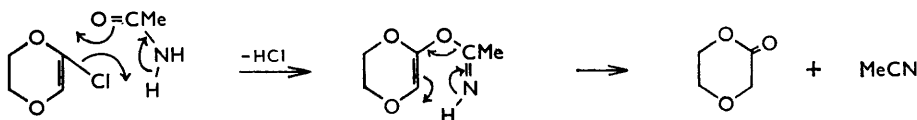
<sup>6</sup> Watanabe, *J. Amer. Chem. Soc.*, 1957, **79**, 2833.

<sup>7</sup> Ruggli, Ratti, and Henzi, *Helv. Chim. Acta*, 1929, **12**, 332.

<sup>8</sup> Astle and Gergel, U.S.P. 2,756,240/1956.

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between this compound and acetamide has been investigated. Again, on heating, there is an exothermic reaction; the products are acetonitrile and 1,4-dioxan-2-one. These products can be accounted for satisfactorily by substitution followed by elimination, as shown.



## EXPERIMENTAL

Melting points are corrected. Ethanol refers to absolute alcohol dried with magnesium. The amines were dried with potassium hydroxide. Dichlorodioxan had m. p. 30–31°.

**Reaction with Cyclohexylamine.**—The dichlorodioxan (39.3 g.) and cyclohexylamine (99.0 g.) were dissolved in ethanol (100 ml.) and left at room temperature for 34 weeks. The precipitated solid (72 g.; moist) gave *sym*-biscyclohexyliminoethane (5.0 g.), m. p. 150–151.5° (from 96% ethanol) (lit.,<sup>9</sup> 149–150°) (Found: C, 76.5; H, 10.8; N, 12.5. Calc. for C<sub>14</sub>H<sub>24</sub>N<sub>2</sub>: C, 76.3; H, 11.0; N, 12.7%). Concentration of the filtrate (at <40°/20 mm.) gave more (4.8 g.) of the Schiff's base; addition of acetone (100 ml.) to the filtrate gave cyclohexylamine hydrochloride (2.4 g.), m. p. and mixed m. p. 210–212° (from acetone–ethanol).

After removal of acetone and alcohol, distillation of the residue gave a fraction (16.9 g.; pale yellow; containing no chlorine), b. p. 25–100°/17 mm.; the remainder did not distil at 160° (bath)/17 mm. and was intractable. The distillate (1.0 g.) in pyridine (0.5 g.) was treated with *p*-nitrobenzoyl chloride (2.0 g.) and gave, as one of the products, a solid insoluble in 4*N*-sodium hydroxide, ethylene glycol bis-*p*-nitrobenzoate (0.7 g.), m. p. and mixed m. p. 142° (from ethanol–water).

**Reaction with Ethylenediamine.**—The dichlorodioxan (78.5 g.) and ethylenediamine (90 g.) were dissolved in ethanol (300 ml.) and left at room temperature for 4 days. The solid (11.6 g.) which separated gave, on crystallisation from methanol, needles of decahydropyrazino[2,3-*b*]pyrazine (Found: C, 50.9; H, 9.8; N, 39.2. Calc. for C<sub>8</sub>H<sub>14</sub>N<sub>4</sub>: C, 50.7; H, 9.9; N, 39.4%); the m. p.s obtained (all with decomposition) depended upon the temperature of insertion, m. p. 162–187° (140°), 200–205° (190°), 200–210° (200°); the purified material always contained traces of chloride ion. The infrared spectrum showed  $\nu_{\max}$ . (Nujol) 870s, 882s, 955s, 1093m, 1150m, 1341m, and 3200s cm<sup>-1</sup>. Acetylation<sup>4</sup> gave needles, m. p. 201–203° (lit.,<sup>4</sup> 202°).

Baganz, Domaschke, and Kirchner give<sup>4</sup> m. p. 195° for the tetra-aza-compound, and Chitwood and McNamee give<sup>5</sup> m. p. 232–234°. Dr. Baganz has carried out a direct comparison of his product with material obtained in the present work, and finds the two samples to be identical [mixed m. p. (167–168.5° without depression), behaviour on paper chromatography, and infrared spectra]. A specimen prepared by the method of Chitwood and McNamee from glyoxal and ethylenediamine had the variable m. p. as described above, and gave an infrared spectrum identical with that previously obtained.

In the preparation from dichlorodioxan, the original mixture, on standing, deposited more solid (50.1 g.) consisting substantially of ethylenediamine hydrochloride; benzoylation gave *NN'*-dibenzoyl ethylenediamine, m. p. and mixed m. p. 255–256°.

**Reaction with Methylaniline.**—The dichlorodioxan (26.1 g.) and the amine (35.6 g.) were dissolved in ethanol (150 ml.). After 36 weeks at room temperature a portion (32 ml.) was treated with a cold solution of picric acid (7.6 g.) in acetone. The mixture was kept at 20°/0.5 mm. for 3 days, and the residue treated with non-aqueous solvents, to yield methylaniline picrate, yellow-green plates, m. p. and mixed m. p. 143–145° (decomp.) (from ethanol) (Found: C, 46.4; H, 3.6; N, 16.4. Calc. for C<sub>13</sub>H<sub>12</sub>N<sub>4</sub>O<sub>7</sub>: C, 46.4; H, 3.3; N, 16.7%).

In another experiment, three times the quantity of amine was used. After 36 weeks a solid (15.2 g.) had separated, and a further quantity (12.1 g.) was obtained by diluting the filtrate with methanol. This did not melt below 250°, contained nitrogen and chloride ion, and yielded, with picric acid in ethanol, methylaniline picrate only, m. p. and mixed m. p. 143–145° (decomp.).

<sup>9</sup> Barry and Mitchell, *J.*, 1953, 3610.

*Reaction between 2-Chloro-5,6-dihydro-1,4-dioxin and Acetamide.*—The chlorodihydrodioxin<sup>8</sup> had b. p. 145—147°/760 mm.,  $n_D^{25}$  1.4662. It (15.1 g.) was heated with acetamide (7.4 g.) at 120° to give a pale yellow solution. On raising the temperature to 130° a vigorous reaction occurred with evolution of hydrogen chloride; the source of heat was immediately removed. Volatile products were passed through a trap cooled in ice-salt. The experiment was repeated six times in all. The total liquid (18.4 g.; pale yellow) in the trap was dried ( $K_2CO_3$ ), and, on repeated distillation, gave acetonitrile (7.2 g.), b. p. 81—82°/760 mm.,  $n_D^{20}$  1.346 (lit.,<sup>10</sup> 1.344), identical (infrared spectrum) with an authentic sample.

The crude mixture, and the pale yellow liquid above, gave, on a 5 mm. × 120 cm. column of 10% of dinonyl phthalate on Celite 545 at 20°, with argon (flow rate 45 ml./min.) as the carrier gas, a chromatogram in which the most volatile component had the same retention time as an authentic sample of acetonitrile. On the same column at 100° no component was detected which had the same retention time as an authentic sample of 2-chloroethyl acetate.

The crude reaction mixtures were combined and heated at 130—140° for 2½ hr. (until evolution of hydrogen chloride had ceased). Distillation gave a fraction (51.2 g.; solid plus liquid) b. p. 93—105°/11 mm., and an intractable residue (44.2 g.) which did not distil at 130° (bath/11 mm. On standing, the distillate solidified; it could not be obtained crystalline, and contained nitrogen and only a trace of chlorine. Trituration of the solid (5.0 g.) with water (6 × 15 ml.) gave a solid (4.54 g.) containing no nitrogen or chlorine;  $\nu_{max}$ . (Nujol) 1745, 1240, 1210, and 1130  $cm^{-1}$ . Distillation from sodium hydroxide (0.5 g.), in apparatus which had been washed with 4N-sodium hydroxide and water and dried at 110°, gave 1,4-dioxan-2-one, b. p. 214—215°/760 mm., m. p. 23—25°. This product could be obtained crystalline when first prepared, but after about 10 days it solidified to non-crystalline material of indefinite m. p. (90—102°), which when redistilled as above gave again a liquid, b. p. 214—215°/760 mm., m. p. 23—25°. A good analysis could not be obtained, but this product gave an infrared spectrum identical with that of authentic 1,4-dioxan-2-one,<sup>11</sup> b. p. 214—215°/760 mm., in the region 4878—500  $cm^{-1}$ .

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<sup>10</sup> Henry, *Bull. Classe Sci., Acad. roy. Belg.*, 1906, 722.

<sup>11</sup> Summerbell and Lunk, *J. Amer. Chem. Soc.*, 1958, **80**, 604.